Abstract

Diabetic nephropathy is one of the major secondary complications of type 2 Diabetes mellitus, which is leading to increased medical burden worldwide. It grows with a variable time or diabetic duration, the progression rate also varies among diabetic patients. Proteinuria is the most trustworthy diagnostic approach. Microalbumin is currently used in clinical diagnosis of incipient nephropathy, but recently its association has been seen with other co-complications which decrease its trustful predictive capabilities. On the other hand urinary IgG has shown its superiority to microalbuminuria in very few studies in last decade. The aim of this thesis was to seek the potential of the putative biomarkers (IgG) for type 2 diabetic nephropathy. The thesis focuses and analyzes urinary excretion of IgG in type 2 diabetic patients.

The first objective was whether IgG is potentially associated with the pool of factor taking responsibility of potential hazards of simple building blocks, carbohydrate protein, lipid and their representatives. The findings have shown odd ratio for the AGEs, AOPP, lipid hydroperoxides and lipid peroxidation products were increased by 5.64 (95% CI 3.52-9.04), 1.03 (95% CI 1.02-1.04), 2.71 (95% CI 2.05-3.57) and 13.72 (95% CI 6.98-26.95) respectively in the diabetic patients group showing high urinary IgG creatinine ratio (UIgGCR). Secondly, odds were calculated for urinary excretion of conventional biomarker microalbumin and putative biomarker IgG in type 2 diabetic patients with other secondary co-complications. The adjusted odds ratio for urinary albumin creatinine ratio (UACR) increased significantly with secondary complications which further increased with declined eGFR up to 1.39 (95% CI 1.26-1.53) p <0.001, the adjusted odds ratio for UACR showed a higher influence on adjustment with other traditional confounders, whereas the odds for U1gGCR was associated with secondary complications in a selective manner. The odds have also shown for the factors affecting renal remodulations. The adjusted odds ratio for the urinary glycosaminoglycan creatinine ratio (UGAGCR) was 1.186 (95% CI 1.061-1.327) p <0.01 in highest quartiles of UIgGCR, followed by odds ratio for markers of collagen catabolism 1.051 (95% CI 1.025-1.079) p <0.001, and urinary sialic acid creatinine ratio (USACR) 1.044 (95% CI 1.013-1.077) p <0.01 respectively. The marker of glycation, i.e glycated hemoglobin had shown the highest odds ratio 5.449 (95% CI 1.132-26.236) p <0.05.

More accurate risk stratification at earlier time points was the main objective of this thesis, patients with fast progression of diabetic nephropathy were identified on the basis of their annual renal function decline. The urinary excretion of microalbumin and IgG were analyzed for their predictive probabilities. The fractional excretion of IgG has shown the higher discriminatory ability for fast declining renal function apparent from the area under curve (AUC) 0.87±0.02 (95% CI 0.83-0.90) which was significantly higher than percentage fractional excretion of albumin, AUC 0.73±0.04 (95% CI 0.68-0.78) p <0.001, with 95.7% sensitivity and 72.3% specificity. These results show that the high UIgGCR is associated with faster deterioration of renal function in type 2 diabetic patients, and fractional excretion of IgG could serve as better marker to stratify the patients on higher risk of end stage diabetic nephropathy.